REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-23, the only claims pending and currently under examination in this application.

Claims 1, 6 and 11 have been amended to recite that the headache pain is caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis. Support for these amendments can be found in the specification, e.g., at page 4, lines 9-13.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

Rejections under 35 U.S.C. §103(a)

Claims 1-23 have been rejected under 35 U.S.C. §103(a) as obvious over Liedtke (US 5,840,755) in view of Drizen et al. (US 5,897,880) and Brand (US 4,681,897) for the asserted reason that Liedtke discloses a method of alleviating headache pain in human subject by applying a topical carrier containing local anesthetics and analgesics to the forehead or temple of a subject in need, which, when coupled with the topical formulations disclosed in Drizen and Brand, renders the claims obvious. However, the Applicants respectfully submit that no reasonable expectation of success is presented in either the references themselves or in the knowledge generally available to one of ordinary skill in the art that would lead one to modify the references or to combine the teachings of the references to make the combination of components as claimed in Claims 1-23 as amended.

A feature of each claim is that a topical NSAID formulation is topically applied to the head of a host in order to provide relief from headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis.

Lietdke teaches a composition for the topical therapy of headaches. The composition contains a local anesthetic, specifically an anesthetic having amide or ester groups, which may be applied to the forehead or temples or both (abstract; col. 2, lines 35-67). However, Lietdke does not teach or suggest compositions that include a NSAID, as claimed in the subject claims. In fact, nowhere in the disclosure of Lietdke is the term "NSAID" even mentioned. Likewise,

Lietdke does not teach that the composition may be employed to treat headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis. Accordingly, Lietdke does not teach or suggest applying a NSAID formulation to a host, let alone applying a NSAID formulation to the head of a host to treat headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis, as claimed in the subject claims.

Drizen et al. teach NSAID formulations, but do not teach or suggest applying such NSAID formulations to the head of a host, as claimed in the subject claims, and instead specifically teach the application of NSAID formulations to the facet joint areas (see for example Test Procudures I, II and III) and the use of diclofenac for the relief of osteoarthritis and associated pain and application of such to sites affected by rheumatic or osteoarthritic disease (see Example 1). Furthermore, Drizen et al. do not teach the treatment of headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis with an NSAID, as claimed in the subject claims. Accordingly, Drizen et al. do not teach or suggest the use of an NSAID formulation applied to the head of a host to treat headache pain, let alone the use of an NSAID formulation to the head of a host to treat headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache and temporal arteritis.

Brand discloses compositions that include capsaicin or an analog thereof and a NSAID drug. However, not only does Brand fail to teach or suggest the use of such compositions to treat headache pain, Brand also fails to teach or suggest the topical administration of the compositions to the head of a subject for the treatment of any disorder, let alone headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache and temporal arteritis, as claimed in the subject claims.

Accordingly, the combination of references fails to teach or suggest the application of a NSAID formulation to the head to treat headache pain and thus fails to teach or suggest the application of a NSAID formulation to the head to treat headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis as these causes of headache pain are not even mentioned in any of the references. Accordingly, the cited references alone or in combination fail to teach or suggest all of the claimed limitations and thus a proper prima facie case of obviousness cannot be made for at least this reason.

Furthermore, modifying the references or combining the teachings of the references to make the combination of components claimed in the instant application fails to provide a reasonable expectation of success.

As described in Applicants' previous response, most illnesses cannot be adequately treated by simply changing the method of application of a formulation. Many formulations are known in the art that are efficient and/or effective at therapeutically relieving an illness by a particular method, but which are inefficient and/or ineffective when applied by a different method. Headache is not exceptional as an illness in this respect. In fact, because so little is known about how headaches are caused and the mechanisms by which drugs successfully treat headaches, their experimental treatment has an extremely variable level of success. Treatments and the methods of administering treatments for headaches are largely empirically determined, and typically a low expectation of success is predicted for a particular composition and method and treatment for a headache.

The expectation of success is further lowered if the therapeutic agent is topically administered, i.e., with little or no systemic activity, as opposed to administered via a different mode. A variety of factors determine whether a drug topically applied will be effective at treating a particular illness such as a headache. For example, it is well known that simply changing the route of administration of a therapeutic agent, e.g., from oral to topical, may prove ineffective and/or inefficient. One important variable in this regard relates to the dosage required for a particular route. Accordingly, topical administration of a drug could result in an insufficiently absorbed amount of the agent such that topical administration would not be effective, or the amount of the drug that may be required to be effective when administered topically may be too great, e.g., may be toxic or produce adverse effects.

Further adding to this low expectation of success is the fact that certain topical drugs may be applied on certain parts of a body and not on others, e.g., some areas of the body may be intolerable to a particular drug or the dosage of a drug that would be necessary to treat a particular illness would be to great for a particular area. Specifically, topical drugs typically need to be topically administered at a location most effective for the particular pain being treated, however, there are locations on a host's body that may not be able to tolerate certain topically applied drugs and/or do not allow sufficient absorption of drug and thus the expectation of

success is further lowered when administering a drug at a different site on the body and particularly a different region of the body such as from the truck to the head. For example, many topically applied drugs are contraindicated for areas of and about mucous membranes such as the eyes, mouth, etc., and/or areas of sensitive skin such as areas where the stratum corneum is relatively thin such as the face, but may be used with success on other parts of the body such as the torso, etc. Furthermore, the effective dose of a particular agent administered to one location may be different from the effective dose for the same agent administered to another location, e.g., due to the skin thickness at the different sites. However, changing dosages to accommodate different locations on a body may prove unsuccessful, e.g., the dosage may be too high, e.g., may be toxic, or may be too low, e.g., when lowering a dosage to accommodate sensitive skin areas.

Furthermore, even in those instances where a therapeutic agent may be administered at various areas on the body without causing adverse reactions or intolerable side effects, the therapeutic agent may not be as effective when applied at some areas as compared to others. This may be particularly true when a therapeutic agent is applied to an area of the body wherein the agent must cross a bone barrier to be effective such as the head. Thus, the same expectation of success cannot be predicted from the application of a particular therapeutic agent to an area that does not include bone barriers and the application to an area that does include bone barriers. In fact, typically a lowered expectation of success can be predicted for a formulation that has to cross bone barriers.

Further adding to the low expectation of the success is the application of a given therapeutic agent to a different area of the body to treat a different type of malady. For example, even if a therapeutic agent is effective at treating a particular type of malady such as a particular type of headache by the application to a particular area of the body, there is no indication that an application of the same therapeutic agent will be effective at treating different types of maladies such as different type of headaches when applied to the same area of the body, let alone effective at treating different types of maladies such as different types of headaches when applied to a different area of the body.

In summary, some therapeutic agents produce desirable results upon topical administration whereas others do not. Furthermore, some drugs produce desirable results upon topical administration to certain areas of the body, but may be ineffective, or even produce

undesirable results, when administered to other areas of the body. Still further, some drugs may be effective at treating a certain malady by application to a particular area of the body, but may be ineffective at treating different types of maladies when applied to the same application area. The expectation of success is further lowered when such a drug is applied to a different area of the body to treat a different type of malady. In other words, a drug applied to one part of the body to treat a particular malady may not be effective at treating the different maladies when applied to this same area, let alone effective at treating different maladies when the are of application is changed.

Although diclofenac gel has been successful at treating some headaches when topically applied to the facet joint area, the expectation of success of an NSAID topically applied to the head to treat even the same headache is very low, let alone applied to a different area of the body (the head) to treat other types of headache pain such as headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache or temporal arteritis as claimed in the subject claims. In fact, topical application of NSAID at facet joint area is most likely only treating one uncommon headache condition, cervicogenic headache, and will have no effect on more common headache conditions, such as tension-type headaches, migraine headaches, sinus headaches, cluster headaches and temporal arteritis headaches, and the like, whereas topical NSAID treatment when applied to the head of a host such as the forehead and/or temples will be able to alleviate tension-type headaches, migraine headaches, sinus headaches, cluster headaches and temporal arteritis headaches, in certain individual sufferers and will unlikely treat patients with cervicogenic headache.

Although the combination of the references suggested by the Examiner may suggest that it would be *obvious to try* using a NSAID formulation on an area of the head to treat headache pain, there is certainly no prediction that the treatment would be so successful, especially in terms of the relative sensitivity of the head, as well as in terms of effectively crossing the bone barrier of the head, such that one would have a reasonable expectation of success and especially for treating headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache and temporal arteritis. Since a reasonable expectation of success is not taught in the combined references, at least this prong of the three prong test of *prima facie* obviousness has also not been met and a proper *prima facie* case of obviousness cannot be made.

Accordingly, the cited combination of references fails to render the claims obvious because (1) the combination of references fails to teach or suggest application of a NSAID to the head to treat headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache and temporal arteritis, and (2) the combination of references fails to provide a reasonable expectation of success of treating headache pain caused by a tension headache, migraine headache, cluster headache, sinus headache and temporal arteritis by applying an NSAID formulation to the head of a host. As such, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, Order No. CALD-007.

Respectfully submitted,
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